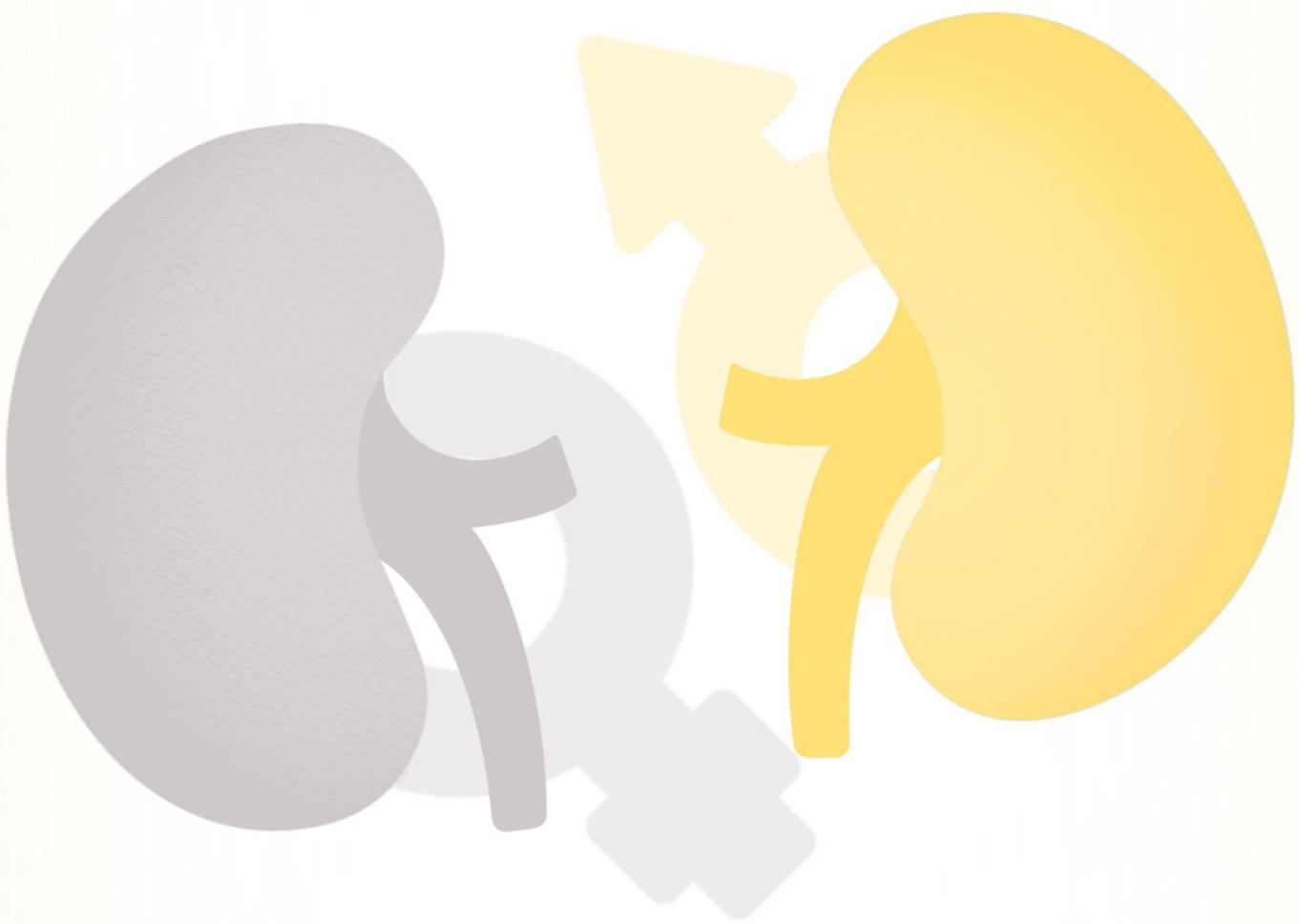


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Physiology



Sheet: Physiology of pregnancy

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PLACENTA AS ENDOCRINE ORGAN

Placenta is not just an organ that provides essential substances for the embryo such as oxygen, glucose and eliminates waste products such as CO₂, but also an endocrine organ that secretes important **hormones** for pregnancy and development of the fetus.

These hormones include Human chorionic gonadotropin (hCG), estrogen, progesterone, human Chorionic Somatomammotropin. (each will be discussed in detail).

Normally if there is no fertilization, menstruation starts 2 weeks after ovulation, but If fertilization took place menstrual sloughing would be prevented by secretion of HCG by the newly developing embryonic tissue. The HCG is first measured in the blood 8~9 days after ovulation and that's when **blastocyst implants** so women can check pregnancy by using pregnancy tests, then HCG reaches its highest level at about week 10 of pregnancy and then decreases to a low level by the 16th-20th week and remains so till the end of pregnancy.

*1-HCG Secreted by placenta. More specifically by syncytial trophoblast cells.

A- **Most important function** is to maintain corpus luteum, so it continues secreting estrogen & progesterone till **13-17 weeks of gestation**.

**after that, placenta will continue to secrete estrogen and progesterone.

Both are important, especially at the beginning of gestation as they maintain the **secretory function** of decidual cells which will be swollen and nutritive to the implanted ovum.

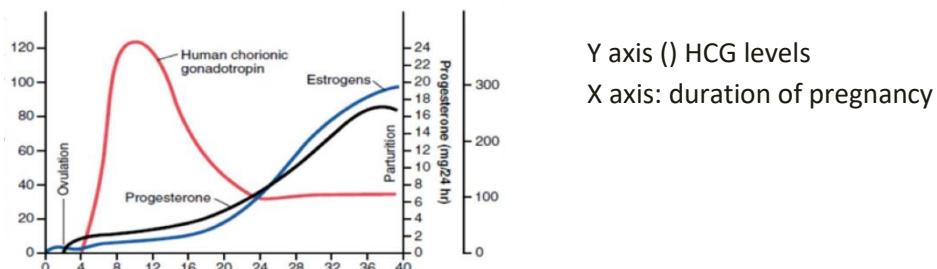
B- second function is important for **male fetus** as it has an **LH** like stimulating effect on Leydig cells in the interstitial cells of testis to secrete testosterone, which is important for male sex organ **growth**. After birth, testosterone secretion by testis will help them to **descend**.

Finally, corpus luteum involutes slowly after the 13th- 17th week of gestation.

What if corpus luteum was removed before 7th week of pregnancy?

Spontaneous abortion will take place due to the decline in estrogen & progesterone levels in blood. But if it occurs after 13th week it will not cause this deleterious effect.

The picture demonstrates different levels of pregnancy hormones, focus on HCG.



*HCG increases after 4th week and continues rising until 10th- 12th week after fertilization then will decline till 20th of pregnancy and remains at this low level to the end of pregnancy. While estrogen and progesterone start low and rise right after reaching HCG its low levels.

2-ESTROGEN

Secreted by syncytial trophoblast cells of placenta. It reaches **30x** of normal levels in female towards the end of pregnancy. Derived from weak androgen (DHEA) released from maternal & fetal adrenal cortices. So, it is not completely synthesized de novo from cholesterol due to the lack of required enzymes in the placenta.

Functions?

- A-**Enlargement of female sex organs (uterus, breast, ductal system & external genitalia)
- B-**Relaxation of pelvic ligaments in preparation for labor (sacroiliac joints, symphysis pubis)
- C-** Activation of the uterus (development of gap junctions)

3-Progesterone

Progesterone is essential for a successful pregnancy; moderate quantities are secreted by corpus luteum at the beginning of pregnancy. Later on and as pregnancy proceeds, larger quantities are secreted by the placenta(10X), by syncytial trophoblast cells using cholesterol.

Effects of progesterone in pregnancy:

1. causes decidual cells to develop in uterine endometrium (provide nutrition for early embryo).
2. decreases contractility of the pregnant uterus, thus preventing spontaneous abortion.
3. contributes to the development of the conceptus before implantation (secretions of the mother's fallopian tubes and uterus to provide nutrition for the developing morula and blastocyst).
4. it's believed that progesterone affects cell cleavage in the early developing embryo.
5. helps estrogen prepare the mother's breasts for lactation after delivery.

4-Human Chorionic Somatomammotropin or Human placental lactogen (hPL)

Protein hormone, secreted by placenta around the 5th gestational week, quantities of hPL secreted are several times greater than that of all the other pregnancy hormones combined.

Functions in the mother (not all are well known)

- 1-Breast development (cannot induce milk in human but do in Animals).
- 2-it has a Weak growth hormone's action (100x less)
- 3-Inhibits insulin sensitivity =↓ Glu utilization by mother which may increase it in fetus instead.
- 4-Promotes release of FA (alternative source of energy for the fetus) Mainly metabolic actions

5-Relaxin

Polypeptide, Secreted by corpus luteum and placenta along with estrogen and progesterone.

Functions in the mother (not well proven)

- A-**Relaxation of symphysis pubic ligament (weak effect)

B-Softens the cervix at delivery.

C- vasodilator (may increase blood flow, venous return, and cardiac output).

CHANGES IN MATERNAL ENDOCRINE SYSTEM:

changes will take place due **to maternal metabolic load or in response to placental hormones**, for example:

1-Anterior pituitary gland enlargement (50%) which increases releasing of ACTH, TSH and PL (corticotropin, thyrotropin, and prolactin). However FSH and LH release is almost totally suppressed—**why..?**— because of the high levels of estrogen and progesterone that will have a negative feedback on anterior pituitary gland in secreting FSH and LH.

2-Adrenal gland Increases **glucocorticoids** secretion leading to an increase in the mobilization of AA required for fetus growth from maternal circulation into fetal circulation. Also, there will be Increased **aldosterone**(2X) (which will retain fluid because of increased NaCl reabsorption leading to what is known as **pregnancy-induced hypertension**).

3-Thyroid gland enlargement (50%) and increases in thyroxine production, which will increase the metabolic rate, also there are some thyrotropic effects of HCG, TSH, and placental human chorionic thyrotropin

4-Parathyroid gland enlargement, especially if the woman suffers from Ca++ deficiency-> Increase PTH secretion (maintain normal Ca+2) to **ossify bones** of fetus.

CHANGES IN DIFFERENT ORGANS

1-Increase in uterine size (50 gm to 1100 gm).

2-The breast doubles in size.

3-The vagina enlarges.

4-Development of edema and acne.

5-Masculine or acromegalic features due to overall growth during pregnancy.

6-Weight gain 10-12 kg (**last 2 trimesters**) (~4kg fetus) due to: weight of fluid (amniotic fluid + increased retention of water) and increased fat deposition.

7-Increase in appetite due to: Removal of nutrients by fetus and hormonal effect .

KIDNEY FUNCTION DURING PREGNANCY

The renal tubules' reabsorption capacity for Na+, Cl-, and water is increased as much as 50% because of:

A-cortical and placenta steroid hormones.

B-The renal blood flow and GFR increase up to 50%.

C- Tubuloglomerular feedback.

D-NO or relaxin.

**Normal pregnant women accumulate about ~2.5 kg of extra water and salt that will be excreted few days after delivery.

Metabolism changes:

A-Increase basal metabolic rate (15%) due to thyroxine, ACTH and sex hormones actions.

B-Increase in daily requirements for: Iron (RBC production for fetus), Phosphates, Ca++(for developing bones) and Vitamins - vitamin D (for Ca+2 absorption from GIT)

CHANGES IN CIRCULATORY SYSTEM (most important changes)

A-Increase in blood flow through the placenta, 625 ml/min

B-Increase in maternal blood volume (30%) due to:

1-Increased aldosterone and estrogen which increases ECF.

2- Increased activity of the bone marrow producing more RBCs.

3- 1-2 L of extra fluid present by the end of pregnancy. The presence of this extra fluid, which is considered an extra safety factor in case the pregnant women lost a lot of blood during her labor (usually 1/2L of blood is lost during delivery)

4-increased fluid retention

C-Blood Flow and Cardiac Output Increase During Pregnancy (30-40%) during 27th week.

Due to increased metabolism and blood flow

D-the cardiac output falls in the last 8 weeks of pregnancy.

Because the blood flow in some other tissue(s) may be reduced.

CHANGES IN RESPIRATION

1-Increase in O₂ consumption (20%)

A- Increased Basal Metabolic Rate because of hormones & fetus demands.

B- Increased body size.

2-Increase in respiratory rate (RR)

A-Progesterone ↑ sensitivity of respiratory center to CO₂.

B- the growing uterus presses upward against the abdomen, which will press against the diaphragm, so the total excursion of the diaphragm is decreased, thus respiratory rate is increased to maintain the extra ventilation.

**As a result, an increase in minute ventilation by 50% and a decrease in arterial PCO₂ to several ml occur.

AMNIOTIC FLUID -Fluid surrounding the baby inside fetus membrane. Its Normal volume is 500ml-1L. (could be more)

-The water in amniotic fluid is replaced once every 3 h, while electrolytes such as (Na⁺, K⁺) are replaced on average once every 15h.

- A large portion of the fluid is derived from renal excretion by the fetus.

-Some absorption occurs by fetus GIT and lungs.

-amniotic **membranes** contribute to its formation, recycling, and absorption.

**even when the fetus dies, amniotic fluid turnover still takes place suggesting contribution of amniotic membrane to the amniotic fluid.

Abnormalities:

1-PREECLAMPSIA

5 % of all pregnant women experience **pregnancy-induced hypertension**, a rapid rise in arterial blood pressure to hypertensive levels during the last few months of pregnancy.

Usually associated with proteinuria.

Characterized by:

- 1-Excess salt and water retention by the mother's kidneys.
- 2-Weight gain, edema, and hypertension in the mother.
- 3-Vascular endothelial function is impaired and arterial spasm that take place in many parts of the mother's body (kidneys, brain, and liver).
- 4-Renal blood flow and GFR are decreased so kidney function will be affected.

Mechanism (theories): 1-excessive secretion of placental or adrenal hormones.

2- some type of autoimmunity or allergy in the mother caused by fetus.

Evidence : Preeclampsia is initiated by insufficient blood supply to the placenta early in pregnancy , resulting in the placenta's release of substances that cause widespread vascular dysfunction to the mother —> ****This takes place when trophoblasts invade the endometrium inducing changes in endometrial arterioles in order to get larger and provide enough blood supply to the developing fetus. So, when maternal arterioles fail to undergo adaptive changes, the blood supply would not be sufficient forcing the placenta to release harmful substances to the vasculature of the mother.**

3- increased levels of inflammatory cytokines such as TNF-α and IL-6.

4- Placental factors that impede angiogenesis (blood vessel growth) has a role.

2-ECLAMPSIA: an extreme degree of preeclampsia in which Vascular spasm occur throughout the body; There may be Clonic seizures in the mother, sometimes followed by coma. Great decrease in kidney output; Liver malfunction; Extreme hypertension. Characterized by a generalized toxic condition of the body. (Very serious) usually occurs shortly before birth.

Without treatment, a high percentage of mothers with eclampsia die. However, with optimal and immediate use of rapidly acting vasodilating agent drugs and then followed by a termination of the pregnancy the mortality rate will be reduced to less distinct than 1%

GOOD LUCK